UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF CHEMICAL SAFETY
AND POLLUTION PREVENTION

July 2013

Subject: Formulation Amendment to Add Alternate CSFs

Dear Applicant:

The amendment referred to above, submitted in connection with registration under the Federal Insecticide, Fungicide and Rodenticide Act (FIFRA), as amended, is not acceptable.

Changes in the product formulation are significant enough such that confirmatory efficacy testing must be addressed.

Background

For new products, confirmatory efficacy data are required for formulations that an applicant manufactures that duplicate a product already registered with complete supporting efficacy data. In such cases, the chemical composition, manufacturing procedure, label claims, and directions for use must be identical in substance to those of the original registration, and specific references (Master Record ID Numbers [MRID]) to the supporting data developed for the original product must be cited by the applicant.

Confirmatory efficacy data are also required for minor formulation changes in an already registered product. In these situations, the change in the formulation is relatively minor, e.g., a change of an inert ingredient.

For minor formulation changes, confirmatory efficacy data are *not* required when a different fragrance is substituted for a fragrance already present in a formulation, or when a different dye is substituted for a dye already present in a formulation. The new fragrance or dye must also be added at the same nominal concentration with the same certified limits as the replaced fragrance or dye to be exempt from confirmatory testing. Additionally, products that are aerosol formulations require confirmatory efficacy data to be submitted for all formulation changes, except the addition or substitution of fragrances. Fragrances for antimicrobial aerosol products making public health claims can be added by notification provided the new fragrance(s) is within the certified limits established for fragrances already approved for the product.

For minor formulation changes, any changes to a product's inert ingredients or their certified limits, other than the circumstances with fragrances and dyes mentioned above, will require

confirmatory efficacy data unless sufficient rationale is presented and accepted by the Agency. Such applications would fall under PRIA and be assigned a PRIA code of A570, have a four (4) month review timeframe, and be assessed a fee of $3,474. Refer to the relevant OCSPP 810 series guideline for specific details on confirmatory testing. Confirmatory efficacy data is required for each use claim (use pattern) identified in the OCSPP 810 series guidelines. Confirmatory efficacy data for viruses may use the hierarchy approach with the hardest to kill virus listed on the label being tested. In addition, products that include *C. difficile* or *Mycobacterium* claims are required to perform full efficacy testing data to support these organisms.

For minor formulation changes, if the agency determines that already submitted/cited product chemistry and/or acute toxicity data cannot be bridged to support the proposed alternate formulation, then that formulation will not be allowed under the existing registration. Central to this determination is a consideration as to whether the product labeling accurately reflects the alternate formulation with respect to its chemical properties and acute toxicity profile. Per 40 CFR Part 152.43,

1) The alternate formulation must have the same certified limits for each active ingredient as the basic formulation.

(2) If the alternate formulation contains an inert ingredient or impurity of toxicological significance, the formulation must have the same upper certified limit for that substance as the basic formulation;

(3) The label text of the alternate formulation product must be identical to that of the basic formulation.

(4) The analytical method required under § 158.355 of this chapter must be suitable for use on both the basic formulation and the alternate formulation.

Confirmatory efficacy studies should be conducted under Good Laboratory Practices (GLP). If not, they should be accompanied with rationale as to why the study, or portions of it, did not comply with GLP to aid the reviewer in determining the impact of non-GLP conductance on study acceptability.

If you have further questions concerning this letter, then please contact

Sincerely,

Product Manager
Antimicrobials Division (7510P)